Remarks

Claims 1-19 were pending for purposes of the instant Office Action, but are cancelled in view of new claim 20-38 presented herein.

Claim 7 (now claim 26) is objected to as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant respectfully traverses this objection. Claim 7 (the subject matter of which is now recited in claim 26) is directed to a method employing the step of administering a particular composition of matter. This administration of the composition requires the composition to include a pharmaceutical carrier – a further limitation that is not required in claim 20 (previously claim 1), from which Claim 26 (formerly claim 7) depends. Applicant believes that this additional requirement for a pharmaceutical carrier in the composition does add a further limitation to independent claim 1 (now 20) and therefore meets the requirements of 37 CFR 1.75(c). This limitation is similar to the limitation of claim 38 (formerly claim 19) that was not cited as being objected to in the current Action. Reconsideration and withdrawal of the objection to claim 7 (now claim 26) is respectfully requested.

Claims 1, 3-8, 11-15 and 18-19 stand rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement. The subject matter of these claims is now respectively recited in claims 20, 22-27, 30-34 and 37-38. These new claim numbers will be used for referencing the claims for purposes in this Reply. As now presented, the claims do not recite the broad genus of "metabolic precursors." Instead, the claim recites that the method employs the step of administering "25-hydroxyvitamin D, or an analog, salt, or derivative thereof".

Analogs, salts or derivatives of 25-hydroxyvitamin D were well known in the art at the time of filing the subject application and are a finite list of compounds that were well

known at the time of the applicant's disclosure. In addition, these newly revised claims convey with reasonable clarity to those skilled in the art that, as of the filing date, the applicant was in possession of the invention as now claimed. Thus, the claims are not directed to a method using a species within the genus that includes *any* prodrug that is converted by the25-hydroxyvitamin D-1-alpha-hydroxylase enzyme; rather, the invention contemplates and encompasses the use of a genus that includes 25-hydroxyvitamin D and the known analogs, salts, or derivatives of 25-hydoxyvitamin D. Support for this amendment is provided in the specification at paragraph 029, and elsewhere within the subject application. Therefore, applicant believes the written description requirement under 35 USC 112, first paragraph, is met for the claims as now presented. It is respectfully urged that the rejection be reconsidered and withdrawn in view of the newly presented claims.

Claims 1-19 (now claims 20-38, respectively) have been further rejected under 35 USC 112, first paragraph, as not enabling for any and/or all tumor cells. The Office Action acknowledges that the claims are enabled for colon, breast, and lymphoma cells. Applicant further asserts that the subject claims are enabled for prostate cells and all other specific cancer or tumor cells recited in the genus listed in original claims 4 and 11. New claims 20 and 30 have been amended to include a recitation of this genus of tumor or cancer cells. Applicant believes that the claims are now enabled under 35 USC 112, first paragraph for the tumor or cancer cells expressly recited therein, and respectfully requests reconsideration and withdrawal of this rejection.

Claims 1, 3-4, 7-8, 10-11 and 14 stand rejected under 35 USC 102(b) as being anticipated by Raina, et al. in view of Haussler, et al. Fist, it is respectfully noted that an anticipation rejection requires that each and every element of the claim be taught in a single reference. Because this rejection relies on a teaching in more than one reference, an anticipation rejection is misplaced and should be withdrawn. Nevertheless, applicant addresses the merits of the Raina, et al. reference as if it were cited separately and properly against the subject claims. Specifically, Raina, et al.

teach about alfacalcidol. Alfacalcidol is, notably, 1-OH-vitamin D_3, a synthetic form of vitamin D in which a hydroxyl (OH) group is added to vitamin D. (Its vitamin D_2 counterpart, 1 alpha-vitamin D_2 is doxcercalciferol). Alfacalcidol is a prodrug and is converted to 1,25-dihydroxyvitamin D by a different enzyme (25-Ohase) in the kidney. This resulting 1,25-dihydroxyvitamin D compound is released into the systemic circulation. Thus, alfacalcidol is fundamentally different from our discovery that prostate and other cells possess 1-Ohase, and convert 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D intraprostatically.

Importantly, unlike alfacalcidol (which is the precursor to 1,25-dihydroxyvitamin D in serum), the discovery that prostate and other cells posses 1-OHase allows them to convert 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D *within* the cancerous organ. This is not only more efficient at delivering the compound to the cell, but is markedly less calcemic since the calcemic effects of 25-hydroxyvitamin D are much lower than that of 1,25 dihydroxyvitamin D and alfacalcidol.

Thus, Raina, et al. are deficient in their teaching of the claimed invention and do not anticipate the subject invention. Moreover, in view of this deficiency of Raina, et al, the Haussler et al. teaching of using 25-hydroxyvitamin D as an alternative to vitamin D, and therefore making its use inherent in the teaching of Raina, et al. does not cure the defects of Raina et al.

Claims 1, 3-4, 7-8, 10-11 and 14 also stand rejected under 35 USC 102(b) as being anticipated by Pence et al. s evidenced by Hsu et al. However, the Office Action acknowledges that Pence et al. teach administration of vitamin D and does not teach administration of 25-hydroxyvitamin D. Administration of vitamin D is *not* the claimed invention. Clearly, the subject invention is directed to administering 25-hydroxyvitamin D, or an analog, salt, or derivative thereof that is clearly not vitamin D, per se. An advantage of the subject method is that vitamin D toxicity is avoided. Regardless of whether vitamin D is administered in sub-toxic doses, as taught in Pence, et al., toxicity

can derive from the well-known vitamin D property of accumulation within the body, primarily by sequestration within fat, over time.

In addition, it is important to recognize another fundamental distinction between the subject invention and the teaching of Pence et al. Pence et al. teach that doses of vitamin D inhibit "colon carcinogenesis," i.e., it prevents normal cells from becoming cancer cells. Pence et al. teach nothing about *inhibiting* tumor cells (cancer cells) that are already present. Carcinogenesis is fundamentally different from cancer therapy (treating cancer cells, i.e., cells that have already gone through part or all of the carcinogenic process). There is correlation between agents that inhibit carcinogenesis and agents that are effective as cancer therapies. In fact, some agents that are carcinogenic are effective as cancer therapies. Thus persons of ordinary skill in the art readily recognize that inhibition of carcinogenesis, is not a proxy for an agent that will be effective as a cancer therapy.

Moreover, Hsu, et al. is not a proper reference against the subject application because it was published in April 2001. The subject application claims a priority date of March 1998 – three years before the Hsu reference became available. Accordingly, Hsu, et al. is not prior art to the subject application and cannot support a proper rejection under 35 USC 102. Reconsideration and withdrawal of the rejection citing Pence et al. and Hsu, et al is respectfully requested.

The Pence et al. and Hsu et al references, have also been cited, further in view of Haussler et al, in the rejection of claims 2 and 9 (now claims 21 and 28, respectively) as being unpatentable under 35 USC 103(a). However, Pence et al. fail as a primary reference against the subject invention because, as stated above, Pence et al. do not teach administration of 25-hydroxyvitamin D, as claimed, nor do they teach inhibition of cancer or tumor cells that have undergone any part of carcinogenesis. Hsu, et al is improperly cited as prior art due to its publication date being well after the priority date claimed for the subject application and therefore cannot be used to correct any defect

of the teaching of Pence et al. The defective teaching of Pence et al. (teaching inhibition of carcinogenesis rather than inhibition of cells that have undergone carcinogenesis) is also not cured by the Haussler et al reference. Accordingly, applicant maintains that the subject invention, as currently claimed would not have been obvious in view of the cited references of Pence, et al. Hsu, et al. or Haussler, et al. whether taken separately or as combined. It is respectfully requested that the rejection of claims 2 and 9 (now claims 21 and 28) under 35 USC 103(a) be reconsidered and withdrawn.

Applicant believes the claims as currently presented in this Amendment are in condition for allowance and respectfully requests such action.

Applicant invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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